ANNALS OF SURGERY
Vol. 236, No. 5, 612–618

Long-Term Results of Distal Pancreatectomy for Chronic Pancreatitis in 90 Patients

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Objective

To determine the indications for distal pancreatectomy for chronic pancreatitis and to evaluate the risks, functional loss, and outcome of the procedure.

Summary Background Data

Chronic pancreatitis is generally associated with continued pain, parenchymal and ductal hypertension. and progressive pancreatic dysfunction, and it is a cause of premature death in patients who receive conservative treatment. Good results have recently been reported by the authors and others for resection of the pancreatic head in this disease, but distal pancreatectomy is a less popular option attended by variable success rates. It remains a logical approach for patients with predominantly left-sided pancreatic disease, however.

Methods

A personal series of 90 patients undergoing distal pancreatectomy for chronic pancreatitis over the last 20 years has been reviewed, with a mean postoperative follow-up of 34 months (range 1–247). Pancreatic function was measured before and after operation in many patients.

Results

Forty-eight of 84 patients available for follow-up had a successful outcome in terms of zero or minimal, intermittent pain. There was one perioperative death, but complications developed in 29 patients, with six early reexplorations. Morbidity was unaffected by associated splenectomy or right-to-left dissection. Late mortality rate over the follow-up period was 10%; most of these late deaths occurred because of failure to abstain from alcohol. Preoperative exocrine function was abnormal in two thirds of those tested and was unchanged at follow-up. Diabetic curves were seen in 10% of patients preoperatively, while there was an additional diabetic morbidity rate of 23% related to the procedure and late onset of diabetes (median duration 27 months) in another 23%. Diabetic onset was related to percentage parenchymal resection as well as splenectomy. Outcome was not clearly dependent on the etiology of pancreatitis or on disease characteristics as assessed by preoperative imaging. However, patients with pseudocyst disease alone did better than other groups. Twenty-one of 36 patients who failed to respond to distal pancreatectomy required further intervention, including completion pancreatectomy, neurolysis, and sphincteroplasty. Thirteen of these 21 patients achieved long-term pain relief after their second procedure.

Conclusions

Distal pancreatectomy for chronic pancreatitis from any etiology can be performed with low mortality and a good outcome in terms of pain relief and return to work in approximately 60% of patients. Little effect is seen on exocrine function of the pancreas, but there is a diabetic risk of 46% over 2 years. Pseudocyst disease is associated with the best outcome, but other manifestations of this disease, including strictures, calcification, and limited concomitant disease in the head of the pancreas, can still be associated with a good outcome.

Chronic pancreatitis is a debilitating disease associated with endocrine and exocrine failure, chronic pain, analgesic addiction, a small risk of carcinomatous change, and premature death. Management[1] involves a multidisciplinary group of surgeons, endocrinologists, gastroenterologists, pain specialists, psychiatrists, and primary health physicians, each with attendant outlays of time and expense. The

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Accepted for publication January 25, 2002.

DOI: 10.1097/01.SLA.0000033039.70348.74

natural history of chronic pancreatitis is one of continued pain, progressive abnormalities of the pancreatic duct and parenchyma, functional insufficiency, and a mortality rate of 22% over 10 years.[1] Alcohol abstinence may or may not alter the course of this progression.[1–4]

Besides denervation procedures, the mainstay of surgical treatment of chronic pancreatitis is either resection or a drainage operation. Up to one third of patients develop an inflammatory mass in the head of pancreas with biliary, pancreatic, duodenal, or even portal vein obstruction.[5] The results of pancreatic head resection indicate that the procedure is safe (<1% mortality[6,7]) and gives good long-term pain relief in up to 92% of such patients.[8–10] The rate of endocrine failure (14%) is low following pancreatic head resection, employment records are over 50%, quality of life is improved, and the use of narcotics and alcohol is reduced.[11,12]

The relative advantages of left-sided resections in the management of chronic pancreatitis remain unclear. There are varying reports for the success of this procedure (up to 88% pain relief), the incidence of pancreatic dysfunction postoperatively, and the appropriate indications.[13–17]

It has been suggested that the head of the pancreas is the "pacemaker" of the disease and that resection of the head would therefore be superior to resection of the body and tail.[18] Yet for those with predominantly left-sided disease, distal pancreatectomy seems a logical approach. The present series represents the largest reported in the literature to date of distal pancreatectomy for the single indication of chronic pancreatitis. The aim of the study was to assess the success of this procedure as well as attempting to clarify the etiological, clinical, or radiologic indications for this operative intervention.

METHODS

Over a 21-year period from 1980 to 2000, 90 consecutive distal pancreatectomies for chronic pancreatitis were performed under the care of one surgeon (R.C.N.W.). Retrospective analysis of these cases was performed using medical records, pathology database access, general practitioner contact, and update via the referring medical team. All patients had a histologic and imaging diagnosis of chronic pancreatitis, and many had concomitant pancreatic dysfunction. All patients who had previously undergone pancreatic head resection were excluded from this series. No patients had pancreatic tumors within the resection specimen.

The median duration of follow-up was 34 months (range 1–247). Eighty-four patients were available for follow-up (excluding those patients who died soon after operation or were lost to follow-up).

Pancreatic endocrine function was tested using a standard oral glucose tolerance test. Diabetes was diagnosed when the fasting glucose level was greater than 6.7 mmol/L and/or the 2-hour glucose level (after a 75-g oral glucose load) was greater than 10 mmol/L. Impaired glucose tolerance was diagnosed if the fasting glucose was below 6.7 mmol/L with a 2-hour level between 6.7 and 10 mmol/L.

Exocrine function was assessed either by the pancreolauryl test (normal > 30%) or 3-day fecal fat estimation (normal < 7 g/d).[19]

The Analyze-It add-on statistical analysis package for Microsoft Excel was used for all analyses. Comparisons between preoperative and follow-up albumin and weight were made using the Student *t* test (two-tailed). All other comparisons were analyzed using either the chi-square test (with Yates' correction for continuity) or the Fisher exact test. Where mean values are given, they are followed by figures for standard error about the mean. For all analyses, significance was taken at the 5% level.

Table 1. ETIOLOGY OF CHRONIC PANCREATITIS IN 90 PATIENTS

Etiologic factor	n
Alcohol	52
Idiopathic	29
Recurrent acute pancreatitis	6
Pancreas divisum	2
Trauma	1
Total	90

RESULTS

Sixty-two men and 28 women (ratio 2.2:1) underwent distal pancreatectomy with a median age at operation of 40 years (range 17–75) and median duration of symptoms 36 months (range 1–300). The median age of men at operation was 40 years (range 17–75) and that of women 41.5 years (range 17–75). The etiology of the chronic pancreatitis was predominantly chronic alcohol abuse (Table 1), while the main indication for resection was pain (Table 2). Preoperative endocrine function was tested by a standard oral glucose tolerance test in 74 patients and exocrine function by a pancreolauryl test (56 patients) or fecal fat analysis (7 patients) in 63 patients. Of the glucose tolerance tests, 61 fell within the normal range and 13 were impaired. Eight

Table 2. INDICATIONS FOR DISTAL PANCREATECTOMY

Indication	n
Pain	56
Pseudocyst	1
Recurrent acute-on-chronic pancreatitis	10
Bleeding (pseudocyst or pseudoaneurysm)	6
Suspected tumor	2
Pain and possible tumor	3
Pain and pseudocysts	12
Total	90

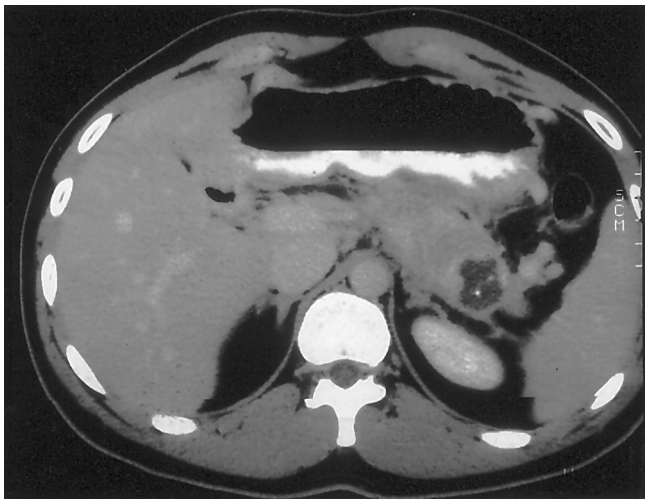

Figure 1. Composite image: CT scan in a 30-year-old man with chronic idiopathic pancreatitis predominantly confined to the body and tail of the gland. The left pancreas is bulky and contains an intrapancreatic pseudocyst with punctate calcification (lower image), while the upper image shows a bulky body of gland with further calcification.

Figure 2. Selective splenic angiogram showing occlusion of the splenic vein and a rich collateral circulation. Splenectomy was combined with distal pancreatectomy in this patient.

patients had already been diagnosed with diabetes preoperatively. Preoperative exocrine function was abnormal in two thirds of patients tested (n = 41).

Thirty-five patients had evidence of pseudocyst formation preoperatively, 31 had calcification of the pancreas, and 25 had strictures of the main pancreatic duct (Fig. 1). Thirty-one patients had clear-cut evidence, on either preoperative imaging or intraoperative examination, of disease in the head of pancreas as well as the body or tail.

Operative Procedure

Median duration of operation was 3.5 hours (range 1.5–7). The 7-hour procedure included construction of a Roux-en-Y loop to a proximal pancreatic pseudocyst.

The spleen was conserved in 29 cases; a right-to-left dissection from neck of pancreas out to spleen was performed in 43 cases, while the operation began with splenic mobilization in the remainder. Splenic preservation was considered in patients in whom imaging and perioperative findings excluded severe pancreatitis with fibrosis around the splenic vessels, gross pancreatic calcification, splenic vein thrombosis, or large distal pseudocysts (Fig. 2).[17] The pancreatic remnant was oversewn in 86 patients; three Roux-en-Y pancreaticojejunostomies were performed for dilated ducts or proximal strictures in the remnant pancreas. Estimation of the percentage pancreatectomy performed was carried out in each case. The amount of pancreas resected was estimated at 40% if the gland was divided to the left border of the portal vein, 50% if in front of the portal vein, 60% along the right border of the vein, and 67% if at the level of the gastroduodenal artery. The median volume of pancreatic resection was 50% (range 10–90%) of the gland. The patient in whom a 10% resection was carried out had an atrophic tail of pancreas with a large pseudocyst in relation to the body of the gland, which was drained.

Morbidity and Mortality

One or more postoperative complications occurred in 29 patients (Table 3). Reexploration was necessary in six (7%) cases: two for postoperative bleeding, one for colonic infarction, two for gastric or small bowel fistula, and one for small bowel infarction. The morbidity rate was 28% for spleen-conserving procedures and 31% for those associated with splenectomy ($P = .93$, Fisher exact test). Right-to-left and left-to-right resections were associated with similar morbidity rates (37% vs. 29%, $P = .59$, Fisher exact test).

Table 3. POSTOPERATIVE COMPLICATIONS

Complication	n
Pancreatic fistula	3
Colonic infarction	1
Gastric fistula	3
Small bowel infarction	1
Deep vein thrombosis	1
Wound infection	3
Intraabdominal collection	9
Chest infection	4
Bleeding	2
Pancreatic abscess	1
Undiagnosed sepsis	1
Total	29

The in-hospital mortality rate was 1%, one patient dying of intraoperative hemorrhage secondary to unrecognized vasculitis in association with fragilitas ossium. Late mortality, which was defined as any death occurring during follow-up of 20 years, was 10%. Of these nine late deaths, three were related to pancreatic disease and had an underlying alcoholic etiology; one patient developed acute pancreatitis at 24 months, one carcinoma of the head of pancreas at 16 months, and the third hypoglycemic coma at 60 months. There was one death from pulmonary embolus during the first postoperative year. The other five deaths were secondary to alcohol abuse and included alcoholic cardiomyopathy (8 years), bleeding duodenal ulcer (7 years), suicide (1 year), hepatic failure (6 years), and alcohol-related pneumonia (2 years). Eight of 52 patients (15%) with an alcoholic etiology died as opposed to 2 of 29 with idiopathic disease (7%) ($P = .45$, Fisher exact test).

Postoperative Outcome

Nutritional Gain

Among 54 patients with available data, there was no significant difference in body weight between values preoperatively and those at follow-up (mean 67.5 ± 2.07 kg vs. 69.4 ± 2.06 kg, $P = .06$). Likewise, among 30 patients, albumin levels were unchanged (39.8 ± 1.27 g/L vs. 37.6 ± 1.16 g/L, $P = .14$).

Pancreatic Function

Among the 89 patients available for postoperative exocrine function testing, 50 of 82 who were tested had an abnormal result, and all but one required replacement therapy. Three patients had normal test results but received pancreatic enzymes for symptomatic insufficiency.

Among 77 patients assessed for postoperative endocrine function testing, 30 had normal glucose curves, 7 had glucose intolerance, and 40 were frankly diabetic. Of these 40 diabetics, 26 were diabetic at immediate in-hospital assessment. However, eight of these patients were already diabetic on preoperative testing. Therefore, there was a diabetic morbidity of 23% related to the surgical resection. The median delay before diabetes in the remainder (n = 14) was 27 months (range 3–60). Of patients who became diabetic postoperatively, eight were controlled with oral hypoglycemics, one was controlled with diet, and four patients became insulin-dependent having been controlled with either diet or oral medication previously. The remainder (n = 27) were insulin-dependent either preoperatively or from the time of diagnosis.

Onset of diabetes was not dependent on gender ($P = .97$, Fisher exact test): 20 of 45 men were diabetic and 10 of 24 women. The size of the pancreatic remnant (unsurprisingly) was significantly associated with the development of diabetes: increased percentage pancreatectomy resulted in more diabetics ($P = .025$, chi-square test, Table 4). Splenic conservation was associated with a reduced incidence of postoperative diabetes ($P = .04$, Fisher exact test, Table 5). Extremes of pancreatic resection were associated with either a very high or low incidence of postoperative diabetes. Excluding the large and small pancreatectomies, where presumably the effect of percentage pancreatectomy is the overwhelming determinant of diabetic outcome, the intermediate pancreatectomies from 34% to 75% were analyzed. In this group the effect of splenic conservation on onset of diabetes was more relevant than that of percentage pancreatectomy (Table 6).

Table 4. ONSET OF DIABETES ACCORDING TO PERCENTAGE PANCREATECTOMY

Diabetic outcome	Percentage Pancreatectomy			
	0–33%	34–50%	51–75%	76–90%
Diabetic (n)	2	13	14	1
Not diabetic (n)	11	20	8	0

$P = .025$.

Pain Relief

Forty patients had no pain, 8 mild or intermittent pain, and 36 relapse of pain. Forty-eight (57%) patients had a lasting response to operation with little or no pain on late follow-up. Patients with recurrent pain had a median response of 12 months (0–108) before symptoms returned.

Of those who were available for assessment, 35 patients were employed at follow-up (including two housewives), with 4 retired. Twenty-seven patients (of employable age) were unemployed because of their medical condition. Of those unemployed, 22 had an underlying alcoholic etiology and 5 were idiopathic ($P = .067$, Fisher exact test). However, pain relief did not reflect etiology ($P = .18$, chi-square test).

When calcification (n = 6), pseudocysts (n = 11), disease extending into the head of the gland (n = 5), strictures (n = 8), or pancreatic atrophy (n = 14) were compared as isolated features, there was a significant improvement in outcome for the pseudocyst group ($P = .008$, chi-square test).

Table 5. INCIDENCE OF DIABETES DEPENDENT ON SPLENIC PRESERVATION

Procedure	Diabetic outcome	
	Diabetes	No diabetes
Splenectomy	18	7
No splenectomy	19	25

$P = .04$.

Table 6. INCIDENCE OF DIABETES IN 34–75% PANCREATECTOMY

Outcome	% Pancreatectomy* 34–50%	51–75%
Diabetes	13	14
No diabetes	20	8
P = .14 Fisher Exact test.		
Procedure/Outcome		
No splenectomy not diabetic	10	0
Splenectomy not diabetic	10	8
No splenectomy diabetic	3	3
Splenectomy diabetic	10	11

P = .04, chi-square test.
* 34–50% resection equates to resections to the left of the portal/superior mesenteric vein tunnel, while those >50% are to the right of the vein.

Pseudocyst disease together with pancreatic ductal strictures occurred in only six cases. Therefore, patients with pseudocysts (generally small in this series) were not considered in the obstructive pancreatopathy group when analyzing symptom control. The atrophic group was the only category of disease in which fewer than 50% of patients were relieved of pain. However, there was no significant difference in pain relief when these different disease features overlapped.

Reoperations

Twenty-one of 36 patients required further pancreatic procedures, including completion pancreatectomy (n = 13), neurolysis (n = 7), and sphincteroplasty (n = 1); the median delay before completion pancreatectomy was 18 months (range 12–72). Of the remaining 15, pain improved spontaneously in 4, remained unchanged in 3, and necessitated opiate analgesia because of deterioration in 8. The one sphincteroplasty was successful in terms of pain relief, but four of the seven patients with neurolysis remain on opiates. Three of the late deaths already described occurred in the completion pancreatectomy group, while all but one of the remaining 10 patients remain free from pain.

DISCUSSION

Pancreatic resection can provide long-term relief from pain associated with chronic pancreatitis as well as full rehabilitation in about half the affected patients. Improved quality of life, return to work, reduced alcohol intake, and reduced analgesic requirements are features of a good response. Although resection of the pancreatic head, either with a pylorus-preserving pancreatoduodenectomy or modified in the Beger's procedure, can produce long-lasting improvement,[5,7,10,12] there are relatively few reports on the results of distal pancreatectomy; pain relief after distal pancreatectomy can vary between 50% and 80% of cases depending on patient selection.[16]

The natural history of chronic pancreatitis is generally one of continuing and progressive debilitation and premature death. Resections for this "benign" condition must be associated with a low mortality rate, especially given the relatively young age of the patients (median age 40 years). The perioperative mortality in our series of 1%, and likewise the complication rate is in line with other reports of distal pancreatectomy for all pathologies (0–0.9%[20,21]). Since several of the complications were serious—there was a reoperation rate of 7%—it was probably the relative youth of the patients that limited the number of deaths. Especially in the presence of pseudocysts and splenic vein thrombosis, distal pancreatectomy for chronic pancreatitis can be a challenging operation and should be performed only in high-volume centers.

One advantage of beginning the operation at the neck of the pancreas and dissecting towards the spleen is that the confluence of the splenic and portal veins is identified at an early stage in case of venous bleeding during posterior mobilization of the body of the pancreas. Approximately half the resections in this series were carried out from right to left, and although no clear advantage could be demonstrated in terms of morbidity, this has become our routine practice.

The late mortality rate of 10% reflects that of other reports.[20] Most late deaths were not secondary to pancreatic causes but represented failure to abstain from alcohol. To improve long-term outcome, attempts at rehabilitation with the involvement of psychiatrists should be considered at the earliest opportunity. Given the incidence of deaths occurring as late as 6 to 8 years after the procedure, attention should be paid to an adequate follow-up in these patients.

The present series achieved a good response with no pain or only occasional mild pain in 57% of patients at a median follow-up of 34 months, a result similar to that of other published series.[13–16] Patients in whom symptoms returned still achieved a median pain-free period of 12 months and a range of up to 9 years. Rehabilitation from operation should not be measured solely in terms of pain-free duration. Unemployment and multiple, expensive hospital admissions are a feature of chronic pancreatitis. In pancreatic head resection, up to 60% of patients may be rehabilitated back to work.[11] In the current series 53% of patients returned to full employment, and another 6% were of retirement age; nevertheless, 41% of those of employable age have not returned to work. The success of the procedure in terms of return to work and pain relief is not dependent on improved nutritional status. Although reports of weight gain exist after pancreatic resection, we found no significant gain in weight or albumin levels despite obvious improvement in symptoms.

Exocrine failure of the pancreas was present in two thirds of those tested preoperatively and remained at this level on follow-up assessment. Distal pancreatic resections, therefore, appear not to influence exocrine function of the pan-

creas in this group of patients, as we have previously noted.[19] By contrast, diabetic curves were present in only 10% of patients preoperatively. Approximately one quarter of patients were rendered diabetic by the procedure alone. Another 18% became diabetic over the following 2 years (31 of 40 insulin-dependent), and this deterioration clearly reflects disease progression as well as the effects of pancreatic resection.

Distal pancreatectomy can be performed with splenic conservation in suitable patients at no increase in terms of complications.[17] Interestingly, a lower incidence of diabetes has been suggested after splenic conservation.[16] There is some experimental evidence for a splenic role in the development of diabetes in certain strains of mice. Interleukin 13 protects these mice from the development of diabetes, and cytotoxic drugs such as cyclophosphamide may cause diabetes at least partly by alterations in splenic T-lymphocyte cytokine expression.[22,23] Both a larger volume of pancreatic resection and splenectomy were associated with a higher incidence of postoperative diabetes. Although the percentage of pancreatic resection was only a rough estimate, there was a good correlation between the extent of pancreatectomy and diabetes, as expected. In the subgroup of patients with a 34% to 75% resection volume, pancreatic volume did not influence the onset of diabetes, while splenic conservation did. It may be that for "borderline" pancreatic resections, the most important factor determining the onset of endocrine failure is the immunologic influence of the spleen.

Some authors have suggested that only patients with obstructive pancreatopathy or pseudocyst disease will achieve long-term pain relief from distal pancreatectomy.[13,16] Alcoholism has also been considered a poor prognostic indicator.[16] In our series the etiology of the disease bore no close relationship to outcome, although the relatively small group of miscellaneous conditions did appear to have a better outcome, with seven of eight patients pain-free at follow-up. In a small series of 20 patients, Warshaw et al. suggested that pseudocyst disease as an indication for distal pancreatectomy was associated with a good outcome.[13] This finding is borne out by the present series, in which the 11 patients (10 pain-free) with pseudocyst disease alone had a significantly better outcome than those with other disease presentations. However, patients with isolated ductal strictures or obstructive pancreatopathy also had a good outcome (seven of eight pain-free). Even patients with chronic calcific pancreatitis or those with obvious disease extending into the head of the gland had at least a 50% chance of pain relief and should therefore not necessarily be excluded from distal resections. The only group in whom a less than 50% success rate was achieved (9 of 14 with poor outcome) comprised patients with chronic atrophic pancreatitis without calcification; perhaps alternative therapeutic options should be preferred in such cases. In most patients, however, pseudocysts, strictures, calcification, and limitation of disease to the head or tail are not features that occur in isolation.

Most patients who developed recurrence of pain required further intervention, one third of them receiving a completion pancreatectomy (15% of entire series) at a median of 18 months. This figure compares to 6 of 52 patients (11%) requiring completion pancreatectomy after pancreatic head resections in our hands after a mean follow-up of 28 months.[24] Less than half of those treated with analgesics alone or a postoperative nerve block had satisfactory pain relief.

In conclusion, distal pancreatectomy for chronic pancreatitis from any etiology can be performed with low mortality and good pain relief in approximately 60% of patients. Many of these patients will be rehabilitated back to work, with no demonstrable effect on exocrine function but a 46% risk of diabetes over the next 2 years. Although the best outcome is seen in patients with pseudocysts and/or disease limited to the left pancreas, some patients with more extensive pancreatitis will still have a good outcome.

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